

## COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name; and

I verily believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: **PEPTIDE NUCLEIC ACID CONJUGATES** the specification of which:

(XX) was filed on October 6, 1995 as International (PCT) Application Serial No. PCT/US95/12931.

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

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I hereby claim foreign priority benefits under 35 U.S.C. § 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of any application on which priority is claimed:

| Country | Number | Date Filed     | Priority Claimed |
|---------|--------|----------------|------------------|
| Denmark | 986/91 | May 24, 1991   | No               |
| Denmark | 987/91 | May 24, 1991   | No               |
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I hereby claim the benefit under 35 U.S.C. § 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of 35 U.S.C. § 112, I acknowledge

the duty to disclose to the U.S. Patent and Trademark Office all information known to be material to patentability as defined in 37 CFR § 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:


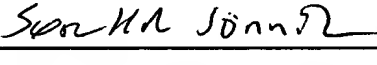

| Application Serial No.                             | Filing Date     | Status (patented, pending) |
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| 08/319,411   | October 6, 1994 | pending                    |
| PCT/EP92/01219<br>(now U.S. Serial No. 08/108,591) | May 22, 1992    | pending                    |
| 08/088,658   | July 2, 1993    | pending                    |
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4 I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: John W. Caldwell and Michael P. Straher, Registration Nos. 28,937 and 38,325 of the firm of WOODCOCK WASHBURN KURTZ MACKIEWICZ & NORRIS, One Liberty Place - 46th Floor, Philadelphia, Pennsylvania 19103, and Herb Boswell and Laurel Bernstein, Registration Nos. 27,311 and 37,280, of ISIS Pharmaceuticals, Inc., 2280 Faraday Avenue, Carlsbad, California 92008.

Address all telephone calls and correspondence to:

Michael P. Straher  
WOODCOCK WASHBURN KURTZ MACKIEWICZ & NORRIS  
One Liberty Place - 46th Floor  
Philadelphia, PA 19103  
Telephone No. 215-568-3100.

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|     |   |  |   |                    |
|-----|---|--|---|--------------------|
| 100 | 1 | Full Name:<br><u>Peter NIELSEN</u>   | Inventor's Signature:<br>   | Date:<br>24/11-85  |
|     |   | Residence: Hjortevanget 509<br>DK 2980 <u>Kokkedal</u> ,<br>Denmark            | Citizenship: Denmark  |                    |
|     |   | Post Office Address: Same as above.  |   |                    |
| 201 | 2 | Full Name:<br><u>Ole BUCHARDT (deceased)</u>                                   | Inventor's Signature:<br><br>Mrs. Dorte BUCHARDT<br>Signing upon<br>information and belief<br>as the Representative<br>of the Estate of Ole<br>BUCHARDT | Date               |
|     |   | Residence: <u>Sondergardsvej 73</u><br>DK 3500 <u>Vaerloose</u> ,<br>Denmark   | Citizenship: Denmark  |                    |
|     |   | Post Office Address: Same as above.  |   |                    |
| 400 | 3 | Full Name:<br><u>Soren Holst SONNICHSEN</u>                                    | Inventor's Signature:<br>   | Date<br>17/12-95   |
|     |   | Residence: <u>Gronhojgardsvej 13</u><br>DK 2630 <u>Tastrup</u> ,<br>Denmark    | Citizenship: Denmark  |                    |
|     |   | Post Office Address: Same as above.  |   |                    |
| 500 | 4 | Full Name:<br><u>Jesper LOHSE</u>  | Inventor's Signature:<br>   | Date<br>15/12/1995 |
|     |   | Residence: <u>Staerevej 52, 2.tv</u><br>DK 2400 <u>Copenhagen N</u><br>Denmark | Citizenship: Denmark  |                    |
|     |   | Post Office Address: Same as above.  |   |                    |
| 600 | 5 | Full Name:<br><u>Michael EGHOLM</u>  | Inventor's Signature:   | Date               |
|     |   | Residence: 1231 Lexington Ridge<br>Drive<br>Lexington,<br>Massachusetts 02173  | Citizenship: Denmark  |                    |
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| 7-00<br>6  | Full Name<br>Muthiah MANOHARAN   | Inventor's Signature | Date |
|            | Residence: 7634 Reposado Drive      Citizenship<br>Carlsbad, California 92009      United States       |                      |      |
|            | Post Office Address: Same as above.  |                      |      |
| 8-00<br>7  | Full Name<br>John KIELY  | Inventor's Signature | Date |
|            | Residence: 4230 Corte Facil      Citizenship<br>San Diego, California 92130      United States         |                      |      |
|            | Post Office Address: Same as above.  |                      |      |
| 9-00<br>8  | Full Name<br>Michael GRIFFITH  | Inventor's Signature | Date |
|            | Residence: 3686 Carmel Landing      Citizenship<br>San Diego, California 92130      United States      |                      |      |
|            | Post Office Address: Same as above.  |                      |      |
| 10-00<br>9 | Full Name<br>Kelly SPRANKLE  | Inventor's Signature | Date |
|            | Residence: 920 Sycamore Avenue, Apt. 61      Citizenship<br>Vista, California 92083      United States |                      |      |
|            | Post Office Address: Same as above.  |                      |      |
| 10         | Full Name  | Inventor's Signature | Date |
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|     |                                     | Residence: Hjortevanget 509<br>DK 2980 Kokkedal,<br>Denmark                   | Citizenship: Denmark   |                      |
|     | Post Office Address: Same as above. |   |  |                      |
| 201 | 2                                   | Full Name:<br>Ole BUCHARDT (deceased)<br><br>311                              | Inventor's Signature:<br><br>D. Bucharde<br>Mrs. Dorte BUCHARDT<br>Signing upon<br>information and belief<br>as the Representative<br>of the Estate of Ole<br>BUCHARDT | Date<br><br>18/11/95 |
|     |                                     | Residence: Sondergardsvej 73<br>DK 3500 Vaerloose,<br>Denmark                 | Citizenship: Denmark   |                      |
|     | Post Office Address: Same as above. |   |  |                      |
| 400 | 3                                   | Full Name:<br>Soren Holst SONNICHSEN  | Inventor's Signature:  | Date                 |
|     |                                     | Residence: Gronhojgardsvej 13<br>DK 2630 Tastrup,<br>Denmark                  | Citizenship: Denmark   |                      |
|     | Post Office Address: Same as above. |   |  |                      |
| 50  | 4                                   | Full Name:<br>Jesper LOHSE  | Inventor's Signature:  | Date                 |
|     |                                     | Residence: Staerevej 52, 2.tv<br>DK 2400 Copenhagen N<br>Denmark              | Citizenship: Denmark   |                      |
|     | Post Office Address: Same as above. |   |  |                      |
| 60  | 5                                   | Full Name:<br>Michael EGHOLM  | Inventor's Signature:  | Date                 |
|     |                                     | Residence: 1231 Lexington Ridge<br>Drive<br>Lexington,<br>Massachusetts 02173 | Citizenship: Denmark   |                      |
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| 70<br>6  | Full Name<br>Muthiah MANOHARAN   | Inventor's Signature | Date |
|          | Residence: 7634 Reposado Drive      Citizenship<br>Carlsbad, California 92009      United States       |                      |      |
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| 80<br>7  | Full Name<br>John KIELY  | Inventor's Signature | Date |
|          | Residence: 4230 Corte Facil      Citizenship<br>San Diego, California 92130      United States         |                      |      |
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| 90<br>8  | Full Name<br>Michael GRIFFITH  | Inventor's Signature | Date |
|          | Residence: 3686 Carmel Landing      Citizenship<br>San Diego, California 92130      United States      |                      |      |
|          | Post Office Address: Same as above.  |                      |      |
| 100<br>9 | Full Name<br>Kelly SPRANKLE  | Inventor's Signature | Date |
|          | Residence: 920 Sycamore Avenue, Apt. 61      Citizenship<br>Vista, California 92083      United States |                      |      |
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|                                     | Peter NIELSEN  |  |             |
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| Post Office Address: Same as above. |  |  |             |
| 2                                   | Full Name:   | Inventor's Signature:  | Date        |
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|                                     | Residence: Sondergardsvej 73<br>DK 3500 Vaerloese,<br>Denmark                    | Citizenship: Denmark   |             |
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| 3                                   | Full Name:   | Inventor's Signature:  | Date        |
|                                     | Soren Holst SONNICHSEN   |  |             |
|                                     | Residence: Gronhojgardsvej 13<br>DK 2630 Tastrup,<br>Denmark                     | Citizenship: Denmark   |             |
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| 4                                   | Full Name:   | Inventor's Signature:  | Date        |
|                                     | Jesper LOHSE   |  |             |
|                                     | Residence: Staerevej 52, 2.tv<br>DK 2400 Copenhagen N<br>Denmark                 | Citizenship: Denmark   |             |
| Post Office Address: Same as above. |  |  |             |
| 5                                   | Full Name:   | Inventor's Signature:  | Date        |
|                                     | Michael EGHOLM   | <i>Michael Egholm</i>  | Nov 9, 1972 |
|                                     | Residence: 1231 Lexington Ridge<br>Drive<br>Lexington, MA<br>Massachusetts 02173 | Citizenship: Denmark   |             |
| Post Office Address: Same as above. |  |  |             |

|           |  |                      |      |
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| 70<br>6   | Full Name<br>Muthiah MANOHARAN   | Inventor's Signature | Date |
|           | Residence: 7634 Reposado Drive      Citizenship<br>Carlsbad, California 92009      United States       |                      |      |
|           | Post Office Address: Same as above.  |                      |      |
| 800<br>7  | Full Name<br>John KIELY  | Inventor's Signature | Date |
|           | Residence: 4230 Corte Facil      Citizenship<br>San Diego, California 92130      United States         |                      |      |
|           | Post Office Address: Same as above.  |                      |      |
| 900<br>8  | Full Name<br>Michael GRIFFITH  | Inventor's Signature | Date |
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|           | Post Office Address: Same as above.  |                      |      |
| 1000<br>9 | Full Name<br>Kelly SPRANKLE  | Inventor's Signature | Date |
|           | Residence: 920 Sycamore Avenue, Apt. 61      Citizenship<br>Vista, California 92083      United States |                      |      |
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|            | Residence: 920 Sycamore Avenue, Apt. 61      Citizenship<br>Vista, California 92083 <i>CA</i> United States |  |                       |
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|            | Residence   | Citizenship                                      |                       |
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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of:

NIELSEN, Peter et al.

International Serial No.: PCT/US95/12931

Filed: October 6, 1995

For: PEPTIDE NUCLEIC ACID CONJUGATES

Assistant Commissioner for Patents  
Washington, DC 20231

Sir:

ASSOCIATE POWER OF ATTORNEY

The undersigned, Michael P. Straher, Registration No. 38,325, of the firm WOODCOCK WASHBURN KURTZ MACKIEWICZ & NORRIS LLP, One Liberty Place - 46th Floor, Philadelphia, Pennsylvania 19103, Attorney and/or Agent for Applicant(s), hereby appoints the following:

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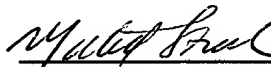
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of ISIS PHARMACEUTICALS, INC., 2280 Faraday Avenue, Carlsbad, California 92008; his associates, with full power to prosecute the above-identified application and to transact all business in the Patent Office connected therewith and requests that correspondence continue to be directed to the firm of WOODCOCK WASHBURN KURTZ MACKIEWICZ & NORRIS LLP at the above address.

Date: April 4, 1997

  
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